

09892613.ST25.txt SEQUENCE LISTING Shawn Shui-on <120> REDUCING IMMUNOGENICITIES OF IMMUNOGLOBULINS BY FRAMEWORK-PATCHING <130> 655 <140> us 09/892,613 <141> 2001-06-27 <160> 71 <170> PatentIn version 3.3 <210> 369 <211> <212> DNA <213> Artificial Sequence <220> FR-patched heavy chaim variable region sequence (Full DNA Sequence) formed by joining the N- and C- terminal (SEQ 3 and 6) <223> halves at the KpeI site. <220> <221> V\_region <222> (1)...(369)<400>

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<210> 2 123 <211> <212> PRT <213> Chimaera sp.

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ile Tyr 20 25 30

Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Page 1

40

Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val 50 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys 85 90 95

Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser 115 120

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<211> 111

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<220>

N-template is a synthetic sense-strand oligonucleotide encoding amino acide 14-50 of the VH region (SEQ ID No. 2). The template is PCR-amplified by two primers (SEQ ID No. 4 and 5)

<220>

<221> V\_region

<222> (1)..(111)

<400> 3

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atgtcttggg ttcgccaggc accgggaaag gggctggagt gggtcgcata c 111

<210> 4

<211> 57

<212> DNA

<213> Artificial Sequence

<220>

<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 1-19 of the VH region (SEQ ID No. 2). The 3' end of the primer overlaps with the 5'end of the template by 18 nucleotides.

<220>

<221> primer\_bind

<222> (1)..(57)

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57

60

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<213> Artificial Sequence
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<223>
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                                                                                          132
gttttgtttg ct
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<213> Artificial Sequence
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<210>	8
<211> <211> <212> <213>	57 DNA Artificial Sequence
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<210> <211> <212> <213>	9 321 DNA Artificial Sequence
<220> <223>	FR-patched light chaim variable region sequence formed by joining the N- and C- terminal (SEQ 11 and 14) halves at the KpeI site.
<220> <221> <222>	V_region (1)(321)
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ggtaagg	gctc cgaaactcct gatctactac actagtatat tacactcagg agtcccatca 180
aggttca	ngtg gcagtgggtc tggaacagaa tttactctca ccattagctc cctgcagcca 240
gaagati	ttg ccacttactt ttgccaacag ggtaatacgc ttccgtggac gttcggtgga 300
ggcacca	aagg tggaaatcaa a 321
<210> <211> <212> <213>	10 107 PRT Chimaera sp.
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Asp Arg	y Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Page 4 40

Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

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Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys 100 105

<210> 11

<211> 108

<212> DNA

<213> Artificial Sequence

<220>

N-template is a synthetic sense-strand oligonucleotide encoding amino acid 11-46 of the VL region (SEQ ID No. 10). The template is PCR-amplified by two primers (SEQ ID No. 12 and 13)

<220>

<221> V\_region

 $\langle 222 \rangle (1)...(108)$ 

<400> 11

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108

60

<210> 12

<211> 51

<212> DNA

<213> Artificial Sequence

<220>

<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 1-17 of the VH region (SEQ ID No 10). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides.

<220>

<221> primer\_bind

<222> (1). (51)

<400> 12

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51

<210> 13

<211> 40

<212> DNA

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         by 18 nucleotides.
<220>
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<221>
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         (1)..(40)
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                                                                                       40
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<221>
        V_region
<222>
        (1)...(120)
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                                                                                      120
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        amino acid 50-65 of the VH region (SEQ ID No. 10). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides
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                                                                                       49
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        16
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<212>
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#### 09892613.ST25.txt 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 92-107 of the VH region (SEQ ID No 10). <223> The primer and the template overlaps by 21 nucleotides. <220> <221> primer\_bind <222> (1)..(48)<400> 16 48 tttgatttcc accttggtgc ctccaccgaa cgtccacgga agcgtatt <210> 17 371 <211> <212> DNA Artificial Sequence <213> <220> FR-patched heavy chaim variable region sequence (Full DNA <223> Sequence) formed by joining the N- and C- terminal (SEQ 19 and 22) halves at the KpeI site. <220> <221> **V\_region** <222> (1)...(371)<400> 17 caggtgcaac tggtggcttc cggggctgag gtaaataagc ctggggcctc agtgaaggtc 60 tcctgcaagg cttctggcta cacatttacc agttacaata tgcactgggt acggcagcct 120 180 cctggaaggg gcctggaatg gattggagct atttatccag gaaatggtga tactagttac aatcagaaat tcaagggcaa ggccacattg actgcagaca aatcctccag cacagcctac 240 300 atgcagctca gcagtctgac atctgaggac tctgcggtct attactgtgc aagatcgcac 360 tacggtagta actacgtaga ctactttgac tactggggcc aaggcaccac tgttacagtc 371 tcctctgatc a <210> 18 <211> 123 <212> PRT <213> Chimaera sp. <400> 18 Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala

Asn Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile 35 40 45

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr

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09892613.ST25.txt
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80
Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp
             100
                                   105
Gly Gln Gly Thr Thr Val Thr Val Ser Ser Asp
<210>
       19
<211>
       114
<212>
       DNA
<213>
       Artificial Sequence
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       N-template is a synthetic sense-strand oligonucleotide encoding
<223>
       amino acide 12-49 of the VH region (SEQ ID No. 18). The template
       is PCR-amplified by two primers (SEQ ID No. 20 and 21)
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<221>
       V_region
<222>
       (1)...(114)
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tacaatatgc actgggtacg gcagcctcct ggaaggggcc tggaatggat tgga
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       57
<212>
       DNA
<213>
       Artificial Sequence
<220>
<223>
       5' Primer is a synthetic sense-strand oligonucleotide encoding
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       nucleotides.
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<222>
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                                                                            57
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       21
<211>
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<212> <213>	DNA Artificial Sequence
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	21 tagt atcaccattt cctggataaa tagctccaat ccattccagg cccct 55
<210> <211> <212> <213>	22 126 DNA Artificial Sequence
<220> <223>	C-terminal is a synthetic sense-strand oligonucleotide encoding amino acid 70-111 of the VH region (SEQ ID No 18) The template is PCR-amplified by tow primers (SEQ ID No 23 and 24)
<220> <221> <222>	V_region (1)(126)
•	22 gcag acaaatcctc cagcacagcc tacatgcagc tcagcagtct gacatctgag 60 gcgg tctattactg tgcaagatcg cactacggta gtaactacgt agactacttt 120
	23 61 DNA Artificial Sequence
<220> <223>	5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 57-76 of the VH region (SEQ ID No 18). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides.
<220> <221> <222>	<pre>primer_bind (1)(61)</pre>
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<211><212><213>	09892613.ST25.txt  59  DNA Artificial Sequence	
<220> <223>	3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 105-123 of the VH region (SEQ ID No 18). The primer and the template overlaps by 21 nucleotides.	
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<210> <211> <212> <213>	25 321 DNA Artificial Sequence	
<220> <223>	FR-patched light chaim variable region sequence (Full DNA Sequence) formed by joining the N- and C- terminal (SEQ 27 and 30) halves at the BspEI site.	
<220> <221> <222>	V_region (1)(321)	
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tcctcc	ccca aaccctggat ttatgccaca tccaacctgg cttccggagt ccctagtcgc 180	
ttcagt	ggca gtgggtctgg gaccgagttc actctcacaa tcagcagttt gcagcctgaa 240	
gatttc	gcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300	
accaagctga ccgttctacg g 321		
<210> <211> <212> <213>	26 107 PRT Chimaera sp.	
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Asp Il	e Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly 5 10 15	
Asp Ar	g Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met 20 25 30	

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr Page  $10\,$ 

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser 50 60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu 65 70 75 80

Asp Phe Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg 100 105

<210> 27

<211> 129

<212> DNA

<213> Artificial Sequence

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<223> N-template is a synthetic sense-strand oligonucleotide encoding amino acide 9-51 of the VL region (SEQ ID No. 26). The template is PCR-amplified by two primers (SEQ ID No. 28 and 29)

<220>

<221> V\_region <222> (1)..(129)

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ttaagtttca tgcactggta ccagcagaag ccaggatcct cccccaaacc ctggatttat 120

gccacatcc 129

<210> 28

<211> 45

<212> DNA

<213> Artificial Sequence

<220>

<220><223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 1-15 of the VH region (SEQ ID No 26). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides.

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<221> primer\_bind

<222> (1)..(45)

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<210> 29

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09892613.ST25.txt
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        by 21 nucleotides.
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                                                                                  40
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                                                                                120
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       Artificial Sequence
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        5' Primer is a synthetic sense-strand oligonucleotide encoding
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       DNA
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       Artificial Sequence
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       primer and the template overlaps by 21 nucleotides.
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Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val 50 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr 65 75 80
Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr
Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ala
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<212>
       PRT
<213>
       Antibody
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Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln 65 70 75 80

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Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 100 105

35 123 <210>

<211>

<213> Immunoglobulin

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35 40 45

Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val 50 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr 65 70 75 80

Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys 85 90 95

Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr 100 105 110

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<210> 41

<211> 11

<212> PRT

<213> Immunoglobulin

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<210> 42

<211> 107

<212> PRT

Immunoglobulin <213>

<400> 42

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Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile 35 40 45

Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln 65 70 75 80

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Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys

<210>

43 23 <211>

<212> **PRT** 

<213> Immunoglobulin

<400> 43

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09892613.ST25.txt
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Asp Arg Val Thr Ile Ser Cys
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Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45
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Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys 85 90 95

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Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser 115 120

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<211> 107

<212> PRT

<213> Immunoglobulin

<400> 48

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile 35 40 45

Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp 85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys 100 105

<210> 49

<211> 123

<212> PRT

<213> Immunoglobulin

<400> 49

O9892613.ST25.txt
Gln Val Gln Leu Arg Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15 Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45 Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe 50 60 Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80 Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95 Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp 100 105 110 Gly Gln Gly Thr Thr Leu Thr Val Ser Ser Asp 115 120 <210> 50 107 <211> Immunoglobulin <213> <400> Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 10 15 Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met 20 25 30 His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser 50 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg 100 105

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51 123 <211>

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<213> Immunoglobulin

<400>

Gln Val Gln Leu Arg Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala 1 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30

Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe 50 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp 100 105 110

Gly Gln Gly Thr Thr Leu Thr Val Ser Ser Asp 115 120

<210> 52

<211> 30

PRT

Immunoglobulin <213>

<400>

Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr 20 25 30

<210> 53

14 <211>

<212> PRT

Immunoglobulin

<400> 53

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly  $1 \hspace{1cm} 5 \hspace{1cm} 10$ 

<210> 54

<211> 32

<212> PRT

<213> Immunoglobulin

<400> 54

Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu 1 5 10 15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg 20 25 30

<210> 55

<211> 32

<212> PRT

<213> Immunoglobulin

<400> 55

Arg Ala Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Asn  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Cys Cys Ala Arg 20 25 30

<210> 56

<211> 11

<212> PRT

<213> Immunoglobulin

<400> 56

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 1 5 10

<210> 57

<211> 107

<212> PRT

<213> Immunoglobulin

<400> 57

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr Page 21 Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser 50 60

40

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr  $85 \hspace{1cm} 90 \hspace{1cm} 95$ 

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg 100 105

<210> 58

<211> 23

<212> PRT

<213> Immunglobulin

<400> 58

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Asp Arg Val Thr Ile Thr Cys

<210> 59

<211> 22

<212> PRT

<213> Immunoglobulin

<400> 59

Asn Leu Met Leu Ile Gln Pro Pro Ser Val Ser Glu Ser Pro Gly Lys  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Thr Val Thr Met Thr Cys 20

<210> 60

<211> 15

<212> PRT

<213> Immunoglobulin

<400> 60

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Pro Val Ile Tyr 10 15

<210> 61

<211> 32

<212> PRT

<213> Immunoglobulin

<400> 61

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys 20 25 30

<210> 62

<211> 32

<212> PRT

<213> Immunoglobulin

<400> 62

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Leu Thr Ile Thr Ser Leu Gln Pro Glu Asp Phe Ala Ala Tyr Phe Cys 20 25 30

<210> 63

<211> 32

<212> PRT

<213> Immunoglobulin

<400> 63

Gly Val Pro Ser Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Phe  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Leu Thr Ile Ser Ser Leu Arg Pro Glu Asp Val Ala Thr Tyr Phe Cys 20 25 30

<210> 64

<211> 32

<212> PRT

<213> Immunoglobulin

<400> 64

Gly Val Pro Ala Arg Phe Ser Gly Tyr Asn Ser Gly Asn Ser Ala Phe
1 10 15

Leu Thr Ile Asn Arg Val Glu Ala Gly Asp Glu Ala Asp Tyr Phe Cys 20 25 30

<210> 65

<211> 11

<212> PRT

<213> Immunoglobulin

<400> 65

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Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
1 5 10
<210>
        66
<211>
        11
<212>
       PRT
       Immunoglobulin
<213>
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<400>

Phe Gly Val Gly Ser Lys Val Glu Ser Lys Arg
1 5 10

<210> 67 <211> 11 <212> PRT <213>

Immunoglobulin

<400>

Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg
1 5 10

<210> 122 <211> <212> PRT <213> Immunoglobulin

<400> 68

Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30

Asn Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile 35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe 50 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp  $100 \hspace{1cm} 105 \hspace{1cm} 110$ 

Gly Gln Gly Thr Thr Val Thr Val Ser Ser

115

<210> 69

<211> 107

<212> **PRT** Immunoglobulin

<400>

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 10 15

120

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser 50 60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu 65 70 75 80

Asp Phe Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg 100 105

<210> 70

122 <211>

<212> **PRT** 

<213> Immunglobulin

<400> 70

Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30

Asn Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile 35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe 50 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr 65 70 75 \_\_ 80 Page 25

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser 115 120

<210> <211> 107

<212> **PRT** 

Immunoglobulin <213>

71 <400>

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly 1 5 10

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met  $20 \hspace{1cm} 25 \hspace{1cm} 30$ 

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Pro Val Ile Tyr 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser 50 60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu 65 70 75 80

Asp Phe Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg 100 105